Please amend Claims 1, 12, 14, 24, 28, 31, 42, 44, 46, 47, 48, and 49. Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i - vii).

1. (Twice Amended) A method for detecting a collection of polymorphisms from nucleic acid molecules in a sample, consisting essentially of the steps of:
   a. obtaining a non-PCR amplified nucleic acid-containing sample;
   b. treating the nucleic acid molecules in said sample to produce a reduced representation of nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:
      i. fractionating said nucleic acid molecules to produce nucleic acid fragments; and
      ii. isolating a subset of said nucleic acid fragments,
      wherein either (i) or (ii) or both (i) and (ii) are performed in a sequence-dependent manner;
   c. detecting pairs of fragments from the same chromosomal location in the reduced representation, wherein pairs of fragments from the same chromosomal location are orthologous sequences; and
   d. comparing orthologous sequences to detect polymorphisms between said sequences,
   thereby detecting a collection of polymorphisms.

12. (Amended) The method of Claim 1, wherein step (b)(ii) is performed by isolating nucleic acid fragments which hybridize to isolated additional nucleic acid sequences.

14. (Twice Amended) A method for detecting a collection of polymorphisms from nucleic acid molecules in a sample, consisting essentially of the steps of:
   a. obtaining a non-PCR amplified nucleic acid-containing sample to be assessed;
   b. treating nucleic acid molecules in said sample to produce a reduced representation of nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:
      i. fractionating said nucleic acid molecules with one or more restriction endonucleases to produce nucleic acid fragments; and
      ii. isolating a subset of said nucleic acid fragments using size fractionation;

wherein either (i) or (ii) or both (i) and (ii) are performed in a sequence-dependent manner;

c. detecting pairs of fragments from the same chromosomal location in the reduced representation, wherein pairs of fragments from the same chromosomal location are orthologous sequences; and

d. comparing orthologous sequences to detect polymorphisms between said orthologous sequences,

thereby detecting a collection of polymorphisms from said nucleic acid molecules.

24. (Amended) The method of Claim 14, wherein step (b)(ii) is performed by isolating nucleic acid fragments which hybridize to isolated additional nucleic acid sequences.

28. (Twice Amended) A method for genotyping a nucleic acid sample to determine the nucleotide present at one or more polymorphic sites of nucleic acid fragments contained in a reduced representation, consisting essentially of the steps of:

a. obtaining a non-PCR amplified nucleic acid-containing sample;

b. treating the nucleic acid molecules in said sample to produce a reduced representation of nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:

i. fractionating said nucleic acid molecules to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments,

wherein either (i) or (ii) or both (i) and (ii) are performed in a sequence-dependent manner; and

c. determining the nucleotide present at one or more polymorphic sites of nucleic acid fragments contained in the reduced representation, thereby genotyping the nucleic acid sample.

31. (Amended) The method of Claim 28, wherein step (b)(ii) is performed by isolating nucleic acid fragments which hybridize to isolated additional nucleic acid sequences.

42. (Twice Amended) The method of Claim 1, wherein step (c) is performed by the following steps:

a. comparing the sequences of pairs of fragments from the reduced representation, wherein if the two sequences are at least 80% identical over at least 80% of the length of the shorter of the two sequences, the two sequences are then aligned;

b. aligning the two sequences identified from (a), wherein if the two sequences are identical over 10 or more contiguous bases within each of the first 50 bases and the last 50 bases of the sequences, the two sequences are compared to determine single nucleotide polymorphisms;

c. determining single nucleotide polymorphisms in the sequences of (b), wherein if the number of single nucleotide polymorphisms does not exceed 1% of the total number of bases in the shorter of the two sequences, the two sequences qualify as a match;

d. repeating (a) - (c) for all pairs of fragments; and

e. determining the number of matches for the same chromosomal location, wherein said matches are accepted if said number of matches does not exceed the theoretical expectations of a binomial or Poisson distribution,

wherein accepted matches are considered a pair.

44. (Twice Amended) The method of Claim 14, wherein step (c) is performed by the following steps:

a. comparing the sequences of pairs of fragments from the reduced representation, wherein if the two sequences are at least 80% identical over at least 80% of the length of the shorter of the two sequences, the two sequences are then aligned;

b. aligning the two sequences identified from (a), wherein if the two sequences are identical over 10 or more contiguous bases within each of the first 50 bases and the last 50 bases of the sequences, the two sequences are compared to determine single nucleotide polymorphisms;

c. determining single nucleotide polymorphisms in the sequences of (b), wherein if the number of single nucleotide polymorphisms does not exceed 1% of the total number of bases in the shorter of the two sequences, the two sequences qualify as a match;

d. repeating (a) - (c) for all pairs of fragments; and

e. determining the number of matches for the same chromosomal location, wherein said matches are accepted if said number of matches does not exceed the theoretical expectations of a binomial or Poisson distribution,

wherein accepted matches are considered a pair.

46. (Twice Amended) A method for determining a population of polymorphisms from nucleic acid molecules in a sample, consisting essentially of the steps of:

a. obtaining a non-PCR amplified nucleic acid-containing sample to be assessed;

b. treating nucleic acid molecules in said sample to produce nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:

i. fractionating said nucleic acid molecules to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments;

wherein either (i) or (ii) or both (i) and (ii) are done in a sequence-dependent manner;

c. isolating from said subset nucleic acid fragments which occur at the same chromosomal locus, thereby producing a pair, and

d. detecting polymorphisms between fragments of a pair;

thereby determining a population of polymorphisms from said nucleic acid-containing sample.

47. (Twice Amended) A method for determining a population of polymorphisms from nucleic acid molecules in a sample, consisting essentially of the steps of:

a. obtaining a non-PCR amplified nucleic acid-containing sample to be assessed;

b. treating nucleic acid molecules in said sample to produce nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:

i. fractionating said nucleic acid molecules with one or more restriction endonucleases to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments using size fractionation;

wherein either (i) or (ii) or both (i) and (ii) are done in a sequence-dependent manner;

c. isolating from said subset nucleic acid fragments which occur at the same chromosomal locus, thereby producing a pair, and

d. detecting polymorphisms between fragments of a pair;

thereby determining a population of polymorphisms from said nucleic acid-containing sample.

48. (Twice Amended) A method for genotyping a nucleic acid-containing sample from an individual to determine the nucleotide present at one or more polymorphic sites, the method consisting essentially of:

a. obtaining a first non-PCR amplified nucleic acid-containing sample to be assessed;

b. treating nucleic acid molecules in said sample to produce a reduced representation of nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:

i. fractionating said nucleic acid molecules to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments;

wherein either (i) or (ii) or both (i) and (ii) are done in a sequence-dependent manner;

c. detecting pairs of fragments from the same chromosomal location in the reduced representation, wherein pairs of fragments from the same chromosomal location are orthologous sequences;

d. comparing orthologous sequences to detect polymorphisms between the orthologous sequences;

e. obtaining a second nucleic acid-containing sample from an individual to be assessed; and

f. determining the nucleotide present at one or more polymorphic sites identified in (d), thereby genotyping a nucleic acid-containing sample from an individual.

49. (Twice Amended) A method according to Claim 48, wherein the second nucleic acid-containing sample is a sample which has been treated by a method comprising:

i. fractionating the nucleic acid molecules in said sample to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments;

wherein either (i) or (ii) or both (i) and (ii) are done in a sequence-dependent manner.

Please add the following new claims:

91. (New) A method for detecting a collection of polymorphisms from nucleic acid molecules in a sample, consisting essentially of the steps of:

a. obtaining a nucleic acid-containing sample;

b. treating the nucleic acid molecules in said sample to produce a reduced representation of nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:

i. fractionating said nucleic acid molecules to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments,

wherein either (i) or (ii) or both (i) and (ii) are performed in a sequence-dependent manner;

c. comparing the sequences of pairs of fragments from the reduced representation, wherein if the two sequences are at least 80% identical over at least 80% of the length of the shorter of the two sequences, the two sequences are then aligned;

d. aligning the two sequences identified from (c), wherein if the two sequences are identical over 10 or more contiguous bases within each of the first 50 bases and the last 50 bases of the sequences, the two sequences are compared to determine single nucleotide polymorphisms;

e. determining single nucleotide polymorphisms in the sequences of (d), wherein if the number of single nucleotide polymorphisms does not exceed 1% of the total number of bases in the shorter of the two sequences, the two sequences qualify as a match;

f. repeating (c) - (e) for all pairs of fragments;

g. determining the number of matches for the same chromosomal location, wherein said matches are accepted if said number of matches does not exceed the theoretical expectations of a binomial or Poisson distribution, wherein accepted matches are considered a pair; and

h. comparing orthologous sequences to detect polymorphisms between said sequences, thereby detecting a collection of polymorphisms.

92. (New) The method of Claim 91, wherein the polymorphisms are single nucleotide polymorphisms.

93. (New) The method of Claim 91, wherein the nucleic acid-containing sample is pooled from more than one individual.

94. (New) The method of Claim 91, wherein the nucleic acid molecules are DNA.

95. (New) The method of Claim 91, wherein the nucleic acid molecules are RNA.

96. (New) The method of Claim 93, wherein the individuals share a trait.

97. (New) The method of Claim 96, where the trait is a disorder.

98. (New) The method of Claim 91, wherein step (b)(i) is performed using one or more restriction endonucleases.

99. (New) The method of Claim 98, wherein the one or more restriction endonucleases are selected from the group consisting of *Bgl*II, *Xho*I, *Eco*RI, *Eco*RV, *Hin*dIII, *Pst*I, and *Hae*III.

100. (New) The method of Claim 91, wherein step (b)(ii) is performed using an agarose gel.

101. (New) The method of Claim 91, wherein step (b)(ii) is performed using high pressure liquid chromatography (HPLC).

102. (New) The method of Claim 91, wherein step (b)(ii) is performed by isolating nucleic acid fragments which hybridize to isolated additional nucleic acid sequences.

103. (New) The method of Claim 91, wherein steps (c-g) and/or step (h) are performed by determining at least a portion of the nucleic acid sequence of the orthologous sequences.

104. (New) A method for detecting a collection of polymorphisms from nucleic acid molecules in a sample, consisting essentially of the steps of:

a. obtaining a nucleic acid-containing sample to be assessed;

b. treating nucleic acid molecules in said sample to produce a reduced representation of nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:

i. fractionating said nucleic acid molecules with one or more restriction endonucleases to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments using size fractionation;

wherein either (i) or (ii) or both (i) and (ii) are performed in a sequence-dependent manner;

c. comparing the sequences of pairs of fragments from the reduced representation, wherein if the two sequences are at least 80% identical over at least 80% of the length of the shorter of the two sequences, the two sequences are then aligned;

d. aligning the two sequences identified from (c), wherein if the two sequences are identical over 10 or more contiguous bases within each of the first 50 bases and the last 50 bases of the sequences, the two sequences are compared to determine single nucleotide polymorphisms;

e. determining single nucleotide polymorphisms in the sequences of (d), wherein if the number of single nucleotide polymorphisms does not exceed 1% of the total number of bases in the shorter of the two sequences, the two sequences qualify as a match;

f. repeating (c) - (e) for all pairs of fragments;

g. determining the number of matches for the same chromosomal location, wherein said matches are accepted if said number of matches does not exceed the theoretical expectations of a binomial or Poisson distribution, wherein accepted matches are considered a pair; and

h. comparing orthologous sequences to detect polymorphisms between said orthologous sequences,

thereby detecting a collection of polymorphisms from said nucleic acid molecules.

105. (New) The method of Claim 104, wherein the polymorphisms are single nucleotide polymorphisms.

106. (New) The method of Claim 104, wherein the nucleic acid-containing sample is pooled from more than one individual.

107. (New) The method of Claim 104, wherein the nucleic acid molecules are DNA.

108. (New) The method of Claim 104, wherein the nucleic acid molecules are RNA.

109. (New) The method of Claim 106, wherein the individuals share a trait.

110. (New) The method of Claim 109, wherein the trait is a disorder.

111. (New) The method of Claim 104, wherein the one or more restriction endonucleases are selected from the group consisting of *Bgl*II, *Xho*I, *Eco*RI, *Eco*RV, *Hind*III, *Pst*I, and *Hae*III.

112. (New) The method of Claim 104, wherein step (b)(ii) is performed using an agarose gel.

113. (New) The method of Claim 104, wherein step (b)(ii) is performed using high pressure liquid chromatography (HPLC).

114. (New) The method of Claim 104, wherein step (b)(ii) is performed by isolating nucleic acid fragments which hybridize to isolated additional nucleic acid sequences.

115. (New) The method of Claim 104, wherein steps (c-e) and/or step (h) are performed by determining at least a portion of the nucleic acid sequence of the orthologous sequences.

116. (New) The method of Claim 104, wherein the subset of (b)(ii) is in a size range selected from the group consisting of: from about 380 base pairs to about 480 base pairs, from about 400 base pairs to about 500 base pairs, from about 480 base pairs to about 580 base pairs, from about 500 base pairs to about 600 base pairs, and from about 540 base pairs to about 640 base pairs.

117. (New) A method for genotyping a nucleic acid sample to determine the nucleotide present at one or more polymorphic sites of nucleic acid fragments contained in a reduced representation, consisting essentially of the steps of:

a. obtaining a nucleic acid-containing sample;

b. treating the nucleic acid molecules in said sample to produce a reduced representation of nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:

i. fractionating said nucleic acid molecules to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments,

wherein either (i) or (ii) or both (i) and (ii) are performed in a sequence-dependent manner;

c. comparing the sequences of pairs of fragments from the reduced representation, wherein if the two sequences are at least 80% identical over at least 80% of the length of the shorter of the two sequences, the two sequences are then aligned;

d. aligning the two sequences identified from (c), wherein if the two sequences are identical over 10 or more contiguous bases within each of the first 50 bases and the last 50 bases of the sequences, the two sequences are compared to determine single nucleotide polymorphisms;

e. determining single nucleotide polymorphisms in the sequences of (d), wherein if the number of single nucleotide polymorphisms does not exceed 1% of the total number of bases in the shorter of the two sequences, the two sequences qualify as a match;

f. repeating (c) - (e) for all pairs of fragments;

g. determining the number of matches for the same chromosomal location, wherein said matches are accepted if said number of matches does not exceed the theoretical expectations of a binomial or Poisson distribution, wherein accepted matches are considered a pair; and

h. determining the nucleotide present at one or more polymorphic sites of nucleic acid fragments contained in the reduced representation, thereby genotyping the nucleic acid sample.

118. (New) The method of Claim 117, wherein step (b)(ii) is performed using an agarose gel.

119. (New) The method of Claim 117, wherein step (b)(ii) is performed using high pressure liquid chromatography (HPLC).

120. (New) The method of Claim 117, wherein step (b)(ii) is performed by isolating nucleic acid fragments which hybridize to isolated additional nucleic acid sequences.

121. (New) The method of Claim 117, wherein steps (c-e) are performed by determining at least a portion of the nucleic acid sequence of the nucleic acid fragments.

122. (New) The method of Claim 117, wherein steps (c-e) are performed by attaching oligonucleotide linker sequences to the fragments in the reduced representation and then amplifying said fragments.

123. (New) The method of Claim 122, wherein the amplification is performed by polymerase chain reaction using primers complementary to the linker sequences.

124. (New) The method of Claim 122, wherein the amplification is performed by cloning the fragments in an organism.

125. (New) The method of Claim 117, wherein steps (c-e) are performed by performing single-base extension reactions on the reduced representation.

126. (New) The method of Claim 117, wherein steps (c-e) are performed by hybridization to an oligonucleotide array.

127. (New) The method of Claim 117, wherein steps (c-e) is performed by an oligo ligation assay.

128. (New) A method for determining a population of polymorphisms from nucleic acid molecules in a sample, consisting essentially of the steps of:

a. obtaining a nucleic acid-containing sample to be assessed;

b. treating nucleic acid molecules in said sample to produce nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:

i. fractionating said nucleic acid molecules to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments;

wherein either (i) or (ii) or both (i) and (ii) are done in a sequence-dependent manner;

c. comparing the sequences of pairs of fragments from the reduced representation, wherein if the two sequences are at least 80% identical over at least 80% of the length of the shorter of the two sequences, the two sequences are then aligned;

d. aligning the two sequences identified from (c), wherein if the two sequences are identical over 10 or more contiguous bases within each of the first 50 bases and the last 50 bases of the sequences, the two sequences are compared to determine single nucleotide polymorphisms;

e. determining single nucleotide polymorphisms in the sequences of (d), wherein if the number of single nucleotide polymorphisms does not exceed 1% of the total number of bases in the shorter of the two sequences, the two sequences qualify as a match;

f. repeating (c) - (e) for all pairs of fragments;

g. determining the number of matches for the same chromosomal location, wherein said matches are accepted if said number of matches does not exceed the theoretical expectations of a binomial or Poisson distribution, wherein accepted matches are considered a pair; and

h. detecting polymorphisms between fragments of a pair;

thereby determining a population of polymorphisms from said nucleic acid-containing sample.

129. (New) A method for determining a population of polymorphisms from nucleic acid molecules in a sample, consisting essentially of the steps of:

a. obtaining a nucleic acid-containing sample to be assessed;

b. treating nucleic acid molecules in said sample to produce nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:

i. fractionating said nucleic acid molecules with one or more restriction endonucleases to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments using size fractionation;

wherein either (i) or (ii) or both (i) and (ii) are done in a sequence-dependent manner;

c. comparing the sequences of pairs of fragments from the reduced representation, wherein if the two sequences are at least 80% identical over at least 80% of the length of the shorter of the two sequences, the two sequences are then aligned;

d. aligning the two sequences identified from (c), wherein if the two sequences are identical over 10 or more contiguous bases within each of the first 50 bases and the last 50 bases of the sequences, the two sequences are compared to determine single nucleotide polymorphisms;

e. determining single nucleotide polymorphisms in the sequences of (d), wherein if the number of single nucleotide polymorphisms does not exceed 1% of the total number of bases in the shorter of the two sequences, the two sequences qualify as a match;

f. repeating (c) - (e) for all pairs of fragments;

g. determining the number of matches for the same chromosomal location, wherein said matches are accepted if said number of matches does not exceed the theoretical expectations of a binomial or Poisson distribution, wherein accepted matches are considered a pair; and

h. detecting polymorphisms between fragments of a pair;

thereby determining a population of polymorphisms from said nucleic acid-containing sample.

130. (New) A method for genotyping a nucleic acid-containing sample from an individual to determine the nucleotide present at one or more polymorphic sites, the method consisting essentially of:

a. obtaining a first nucleic acid-containing sample to be assessed;

b. treating nucleic acid molecules in said sample to produce a reduced representation of nucleic acid fragments isolated in a sequence-dependent manner by a method comprising:

i. fractionating said nucleic acid molecules to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments;

wherein either (i) or (ii) or both (i) and (ii) are done in a sequence-dependent manner;

c. comparing the sequences of pairs of fragments from the reduced representation, wherein if the two sequences are at least 80% identical over at least 80% of the length of the shorter of the two sequences, the two sequences are then aligned;

d. aligning the two sequences identified from (c), wherein if the two sequences are identical over 10 or more contiguous bases within each of the first 50 bases and the last 50 bases of the sequences, the two sequences are compared to determine single nucleotide polymorphisms;

e. determining single nucleotide polymorphisms in the sequences of (d), wherein if the number of single nucleotide polymorphisms does not exceed 1% of the total number of bases in the shorter of the two sequences, the two sequences qualify as a match;

f. repeating (c) - (e) for all pairs of fragments;

g. determining the number of matches for the same chromosomal location, wherein said matches are accepted if said number of matches does not exceed the theoretical expectations of a binomial or Poisson distribution, wherein accepted matches are considered a pair;

h. comparing orthologous sequences to detect polymorphisms between the orthologous sequences;

e. obtaining a second nucleic acid-containing sample from an individual to be assessed; and

f. determining the nucleotide present at one or more polymorphic sites identified in (h), thereby genotyping a nucleic acid-containing sample from an individual.

131. (New) A method according to Claim 130, wherein the second nucleic acid-containing sample is a sample which has been treated by a method comprising:

i. fractionating the nucleic acid molecules in said sample to produce nucleic acid fragments; and

ii. isolating a subset of said nucleic acid fragments;

wherein either (i) or (ii) or both (i) and (ii) are done in a sequence-dependent manner.